

Neuroimaging Biomarkers in Motoric Cognitive Risk Syndrome: A Systematic Review of Structural, Functional, and Molecular Correlates

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Abstract

Background: Motoric cognitive risk (MCR) syndrome is an operationally defined predementia syndrome characterized by slow gait and cognitive complaints. We aimed to systematically synthesize evidence from neuroimaging modalities, including structural, functional, and molecular imaging, to elucidate the biological mechanisms underlying MCR.

Methods: We searched PubMed, Embase, CINAHL, and Web of Science from inception to March 2025, with an update in June 2026. Studies reporting neuroimaging measures in individuals with MCR compared to those without were included. Data were extracted independently by two reviewers. Methodological quality was assessed using the Joanna Briggs Institute Checklist for Analytical Cross-Sectional Studies. A narrative synthesis was conducted following the Synthesis Without Meta-Analysis (SWiM) guidelines.

Results: Twenty-one studies were included, encompassing a total screening pool of 25,515 older adults, with neuroimaging data available for 15,657. All 21 studies employed a cross-sectional design; no study reported a longitudinal neuroimaging analysis. Across ten structural MRI studies, MCR was consistently associated with smaller grey matter volumes or thinner cortex in prefrontal, premotor, insular, and parietal regions, with sex-stratified analysis showing frontal involvement in males and hippocampal involvement in females. White matter hyperintensities and cerebral small vessel disease markers were positively associated with MCR in seven studies. Three diffusion tensor imaging studies revealed widespread white matter microstructural disruption. Two positron emission tomography studies and one plasma-biomarker study consistently found no elevation of Alzheimer's disease (AD) pathology in MCR, distinguishing it from mild cognitive impairment. Two functional near-infrared spectroscopy studies and one electroencephalography study reported prefrontal hyperactivation during dual-task walking and increased frontal theta power, suggesting compensatory neural processes. Eighteen studies (86%) were rated as low risk of bias.

Conclusions:

MCR is associated with a consistent neuroimaging profile characterized by frontoparietal cortical atrophy, cerebral small vessel disease, and absent AD pathology. These findings distinguish MCR from mild cognitive impairment and suggest that disruption of mobility–cognition neural networks, potentially driven by vascular brain injury, may underlie its pathogenesis. Longitudinal studies are needed to establish the temporal and causal nature of these associations.

Registration: PROSPERO CRD420251011713.

1. Introduction

Motoric cognitive risk (MCR) syndrome is a predementia syndrome characterized by the coexistence of slow gait and cognitive complaints in older adults without dementia or mobility disability¹. Unlike mild cognitive impairment (MCI), which requires objective neuropsychological testing for diagnosis, MCR can be identified through a timed walk and a brief cognitive complaint question, making it feasible across diverse clinical and resource-limited settings². Epidemiological studies from 17 countries have estimated the global prevalence of MCR at approximately 9.7%, with an incidence of 65.2 per 1,000 person-years². MCR has been associated with a two- to three-fold increased risk of incident dementia, including both Alzheimer's disease (AD) and vascular dementia, as well as elevated risks of falls, disability, and mortality^{2–4}. With the global population aged 60 years and older projected to reach 2.1 billion by 2050 and dementia prevalence rising correspondingly, the need for simple, scalable screening tools such as MCR is of growing public health importance.

However, MCR is an operationally defined syndrome rather than a biologically defined disease entity. The requirement for only slow gait and cognitive complaints has contributed to uncertainty regarding its underlying mechanisms and the extent to which it reflects specific neurodegenerative, vascular, or mixed pathophysiological processes. Establishing the biological correlates of MCR is therefore essential for validating the construct, refining risk stratification, and clarifying its relationship to other predementia syndromes, particularly mild cognitive impairment (MCI).

Gait speed is a well-established biomarker of health and survival in older adults⁵. Converging evidence indicates that gait and cognition are interdependent rather than independent domains of function. Normal walking engages higher-order cognitive control involving attention, executive function, and motor planning, supported by overlapping neural networks centered on the prefrontal cortex, frontostriatal circuits, and cerebellar-thalamic pathways⁶. Over the past decade, studies have examined neuroimaging correlates of MCR using structural MRI, diffusion tensor imaging (DTI), positron emission tomography (PET), functional near-infrared spectroscopy (fNIRS), and electroencephalography (EEG), covering regional brain volumes and cortical thickness, white matter hyperintensities (WMH) and cerebral small vessel disease (CSVD) markers, microstructural integrity, amyloid and tau pathology, and hemodynamic and neural responses^{3,7–10}.

Despite these emerging trends, individual neuroimaging studies have yielded highly disparate and frequently conflicting results regarding the true neural signature of MCR. For instance, while structural MRI studies report grey matter reductions restricted to frontoparietal motor control networks^{3,7,11–13}, large population-based community cohorts paradoxically extend these structural changes to the hippocampus^{4,14}, a region classically tied to neurodegeneration rather than motor decline. Similarly, the structural relationship between MCR and white matter disease remains unresolved; CSVD markers and WMH are robustly coupled with MCR in community-dwelling samples^{3,8,15}, yet clinical and memory clinic-based samples frequently report completely null associations¹⁶. In the functional domain, observations of prefrontal hyperactivation during dual-task walking¹⁰ and shifted frontal theta

power on EEG⁹ are often framed as compensatory neural mechanisms, but these interpretations remain speculative given the lack of replication across diverse imaging protocols.

These conflicting findings are heavily driven by substantial methodological heterogeneity and architectural limitations across the primary literature. First, because MCR is an operational construct, studies vary drastically in how they define its core components: gait speed thresholds range from population-normalized cut-offs (1 standard deviation below age- and sex-matched norms)^{1,2} to fixed absolute cut-offs drawn from the broader gait-speed literature in older adults (e.g., < 1.0 m/s)^{17,18}, while cognitive complaints are captured using unharmonized instruments ranging from single-item depression scale questions² to multi-domain informant reports^{9,14}. Second, the field is structurally bottlenecked by sample constraints; functional (fNIRS, EEG) and molecular (PET) imaging studies are severely limited by modest, single-center sample sizes that lack the statistical power to adjust for critical vascular or age-related confounders. In contrast, the largest available structural MRI datasets are heavily centralized within the core MCR-Neuroimaging Consortium^{11–13,15,19}. This creates a hidden issue of cohort overlap, where multiple publications draw from identical parent populations, artificially inflating the perceived consensus in the field while limiting true independent replication. Consequently, there is a critical public health and clinical need to systematically appraise and untangle this fragmented literature base. Understanding whether MCR reflects a uniform, frontoparietal vascular prodrome, a mixed neurodegenerative pathway, or a collection of distinct neuroanatomical subtypes requires a comprehensive synthesis that looks beyond isolated modalities. A 2019 systematic review by Sekhon and colleagues partially addressed this gap but drew on only four structural MRI studies available at the time²⁰. That work pre-dates the recent, rapid expansion of MCR imaging research and completely omitted DTI, PET, fNIRS, EEG, and emerging sex-stratified structural trends, all of which have since become critical to the field's clinical interpretation.

By systematically integrating evidence across structural, functional, and molecular modalities, this review aims to map the comprehensive neurobiological footprint of MCR. Specifically, we aimed to: (1) characterize structural alterations associated with MCR; (2) evaluate evidence for white matter pathology; (3) assess molecular imaging evidence for AD pathology; (4) examine functional neuroimaging correlates; and (5) compare neuroimaging profiles of MCR with those of MCI where direct comparisons were available.

2. Methods

2.1. Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement²¹. The protocol was registered on PROSPERO (CRD420251011713) on March 18, 2025. Given the heterogeneity of neuroimaging modalities, outcome measures, and brain regions across studies, a narrative synthesis approach was adopted following the Synthesis Without Meta-Analysis (SWiM) reporting guidelines²².

2.2. Search Strategy

We searched four electronic databases, PubMed, Embase, CINAHL, and Web of Science, from inception to March 2025 using a Boolean search strategy combining two conceptual blocks: (1) neuroimaging terms covering structural MRI, functional MRI, diffusion tensor imaging, positron emission tomography, single-photon emission computed tomography, electroencephalography, magnetoencephalography, functional near-infrared spectroscopy, and specific imaging markers (WMH, gray matter, hippocampal volume, cortical thickness, brain atrophy, cerebral microbleeds); and (2) MCR-related terms including “motoric cognitive risk syndrome,” “MCR syndrome,” “motoric cognitive risk,” and “motoric cognitive syndrome.” The full search strings for each database are provided in the Supplementary Material. A search update was conducted in June 2026 using identical search strings with a 2025–2026 publication year filter to capture studies published since the original search. No language restrictions were applied at the search stage.

2.3. Eligibility Criteria

Studies were included if they met the following criteria: (1) included community-dwelling or clinic-based older adults with MCR syndrome defined per established criteria^{1,2}, characterized by the presence of objectively measured slow gait and cognitive complaints in the absence of dementia or mobility disability; (2) reported at least one neuroimaging measure as a study outcome; (3) employed a cross-sectional, cohort (baseline data), or nested case-control design; and (4) included a comparison group of participants without MCR or examined MCR against a reference standard. Studies were excluded if they were conference abstracts, review articles, editorials, case reports, or did not report neuroimaging data. Studies reporting MCR prevalence without neuroimaging outcomes were retained for epidemiological context but excluded from the imaging synthesis.

2.4. Study Selection and Data Extraction

Records from all databases were exported and deduplicated using Covidence. Two reviewers (S.F. and K.C.) independently screened titles and abstracts against the eligibility criteria. Full texts of potentially eligible studies were retrieved and independently assessed by the same two reviewers. Disagreements at any stage were resolved through consensus discussion.

Data were extracted independently by two reviewers (S.F. and K.C.) using a standardized extraction form developed for this review. The form captured: (a) study identification (author, year, country, cohort, funding); (b) study design and MCR operationalization (gait speed measurement protocol, cognitive complaint instrument, thresholds); (c) participant characteristics (sample size, age, sex, education, cognitive status, comorbidities); (d) neuroimaging acquisition and processing parameters (field strength, scanner, sequences, software, segmentation methods); (e) neuroimaging outcome data (regional brain volumes, WMH burden, diffusion metrics, amyloid and tau PET measures, functional activation patterns); and (f) key findings and effect estimates.

2.5. Risk of Bias Assessment

Methodological quality was assessed independently by two reviewers using the Joanna Briggs Institute (JBI) Checklist for Analytical Cross-Sectional Studies²³. This 8-item tool evaluates the clarity of inclusion criteria, the detail of subject and setting description, the reliability of exposure (MCR) and outcome (neuroimaging) measurement, the identification of and adjustment for confounding factors, and the appropriateness of statistical analyses. Each item was rated as “yes” (low risk), “no” (high risk), “unclear,” or “not applicable.” Studies were classified as having low risk of bias ($\geq 70\%$ “yes” responses), moderate risk of bias (50–69% “yes”), or high risk of bias ($< 50\%$ “yes”). Inter-rater agreement was quantified using Gwet’s first-order chance-corrected agreement coefficient (AC1)²⁴, which is robust to imbalanced category prevalence in JBI-style ratings. AC1 magnitudes were interpreted using the bands of Landis and Koch²⁵. Disagreements were resolved through consensus discussion.

2.6. Data Synthesis

Given the substantial heterogeneity in neuroimaging modalities, brain regions examined, outcome metrics, and MCR operationalizations across the included studies, a narrative synthesis was conducted following the SWiM reporting guidelines²². Studies were grouped by neuroimaging modality for synthesis: structural MRI (volumetric and cortical thickness), WMH and CSVD, DTI, PET, fNIRS, and EEG. Within each modality, we assessed the direction and consistency of associations with MCR using vote-counting based on the direction of effect, applying standard thresholds: consistent evidence ($\geq 70\%$ of studies showing the same direction), suggestive evidence (50–69%), and no clear pattern ($< 50\%$). Evidence summary tables were constructed to present findings by brain region and imaging measure. Where studies directly compared MCR with MCI within the same cohort, these comparisons were synthesized narratively. Sex-stratified analyses were synthesized separately where reported.

3. Results

3.1. Study Selection

The database search yielded 908 records (PubMed: 441, Embase: 389, CINAHL: 12, Web of Science: 66). After removing 477 duplicates, 431 records were screened at title and abstract level, of which 404 were excluded. Twenty-seven full-text articles were assessed for eligibility, and six were excluded (conference abstracts: 3; review article: 1; no extractable quantitative imaging measure: 2). Twenty-one studies met the inclusion criteria and were included in the narrative synthesis (Fig. 1).

3.2. Study Characteristics

The 21 included studies comprised a total screening pool of 25,515 participants (median sample size per study: 358; range: 19–5,023), with neuroimaging data available for 15,657 individuals. Study characteristics are summarized in Table 1. Studies were conducted in single-country USA cohorts (n = 3), single-country European cohorts (France, Netherlands, Switzerland: n = 3), single-country Asian cohorts (Japan, China, South Korea, India: n = 8), and multicontinental consortia (n = 7). Eight studies were community-based, five were clinic-based (memory clinic), and eight employed pooled consortium cohorts or mixed clinic-and-community recruitment. MCR prevalence ranged from 5.0%³ to 40.0%²⁶. All 21 studies employed a cross-sectional design, and no included study reported a longitudinal neuroimaging analysis tracking change in brain structure or function over time. Neuroimaging modalities examined included structural MRI with volumetric or cortical thickness analysis (n = 10), WMH or CSVD markers (n = 7), DTI (n = 3), PET (n = 2), fNIRS (n = 2), and EEG (n = 1). One study reported plasma biomarkers alongside neuroimaging¹⁴.

Table 1. Study characteristics of included studies.

Authors (year)	N	Imaging-analysis N (MCR n / non-MCR n)	Design	Participant characteristics	Cohort / Setting	Country	Imaging modality	Key neuroimaging findings
Beauchet et al. (2016) ⁷	171	171 (28 / 143)	Cross-sectional	Mean age 70.3 years; 37% female; memory clinic	GAIT study, Angers University Memory Clinic	France	Magnetic resonance imaging (3D T1-weighted; FreeSurfer volumetric segmentation)	Smaller total cortical grey matter, premotor cortex, prefrontal cortex, and dorsolateral prefrontal cortex volumes were associated with MCR; premotor cortex showed the largest effect size
Blumen et al. (2019) ¹¹	267	267 (38 / 229)	Cross-sectional	Mean age 75.6 years; 51% female; three cohorts (two community, one memory clinic)	CCMA study, Einstein Aging Study, GAIT study	USA, France	Magnetic resonance imaging (voxel-based morphometry; multivariate covariance analysis)	A grey matter volume covariance network encompassing supplementary motor area, insula, and prefrontal cortex was associated with MCR, independent of age, sex, education, and mild cognitive impairment status
Blumen et al. (2021) ¹²	199	199 (66 / 133)	Cross-sectional	Mean age 72.6 years; 48% female; four cohorts (three community, one memory clinic)	MCR-Neuroimaging Consortium (CCMA, TASCOG, GAIT, NCGG-SGS)	USA, Australia, France, Japan	Magnetic resonance imaging (FreeSurfer cortical thickness, volume, and surface area across 34 regions)	Pervasive cortical thinning was associated with MCR across prefrontal, insular, temporal, and parietal regions; cortical thickness was more sensitive to MCR-related atrophy than cortical volume or surface area
Blumen et al. (2025) ¹⁹	2,048	2,048 (187 / 1,861)	Cross-sectional	Mean age 71.0 years; 46% female; six cohorts	MCR-Neuroimaging Consortium (CCMA, LonGenity, GAIT, TASCOG, KES, NCGG-SGS)	USA, France, Australia, India, Japan	Magnetic resonance imaging (FreeSurfer frontal cortical thickness, hippocampal subfield volumes; sex-stratified analysis)	Males with MCR showed frontal cortical thinning (pars orbitalis and caudal middle frontal); females with MCR showed hippocampal subfield atrophy (CA1, subiculum, granular cell layer of dentate gyrus); sex-specific dissociation was independent of age, education, and vascular comorbidities
Bommarito et al. (2022) ²⁶	20	20 (8 / 12); DTI sub-set 19	Cross-sectional (pilot)	Mean age 74.0 years; 35% female; memory clinic	Geneva Memory Center	Switzerland	Positron emission tomography (amyloid and tau), magnetic resonance imaging, diffusion tensor imaging	Amyloid and tau deposition were not elevated in MCR; lateral ventricular volume was higher and diffusion tensor metrics in the superior corona

Authors (year)	N	Imaging-analysis N (MCR n / non-MCR n)	Design	Participant characteristics	Cohort / Setting	Country	Imaging modality	Key neuroimaging findings
								radiata were altered in participants with MCR
da Costa et al. (2025) ²⁷	19	19 (19 MCR only; no control group)	Cross-sectional	Mean age 74.3 years; 74% female; senior center	Community-based clinical trial (NCT03750682)	USA	Functional near-infrared spectroscopy (prefrontal cortex oxygenation during cycling exercise)	Prefrontal cortex oxygenation showed a non-significant trend toward increase during exercise (p = 0.124); no control group was included
Doi et al. (2022) ⁸	1,227	1,227 (61 / 1,166)	Cross-sectional	Mean age 72.0 years; 53% female; community-dwelling	National Center for Geriatrics and Gerontology Study of Geriatric Syndromes	Japan	Magnetic resonance imaging (modified Fazekas scale for WMH)	Severe WMH (modified Fazekas grade 3 to 4) were independently associated with MCR (odds ratio 2.18; 95% confidence interval 1.15 to 4.16)
Gomez et al. (2022) ³	5,023	1,591 (≈80 / ≈1,511; MCR prevalence in MRI sub-sample = 5%)	Cross-sectional	Mean age 75.1 years; 41% female; community-based	Atherosclerosis Risk in Communities Study	USA	Magnetic resonance imaging, diffusion tensor imaging, florbetapir positron emission tomography	Frontal and parietal lobe atrophy and WMH burden were more pronounced in MCR than in mild cognitive impairment; amyloid deposition was elevated only in mild cognitive impairment, not in MCR
Han et al. (2025) ¹⁴	5,021	1,159 (115 / 1,044)	Cross-sectional	Mean age 70.3 years; 56% female; population-based	Multimodal Interventions to Delay Dementia and Disability in Rural China (MIND-China)	China	Magnetic resonance imaging (volumetric segmentation, voxel-based morphometry, WMH) and plasma biomarkers (amyloid-beta, total tau, neurofilament light)	Smaller volumes of total brain tissue, thalamus, hippocampus, cerebellum, insula, supplementary motor area, and inferior frontal gyrus, and higher WMH volume were associated with MCR; plasma AD biomarkers were not associated with MCR
Mergeche et al. (2016) ¹⁶	358	358 (74 / 284; French 34 / 140, Indian 40 / 144)	Cross-sectional	Mean age 68.4 years; 41% female; memory clinic and community	GAIT study + Kerala-Einstein study	France, India	Magnetic resonance imaging (FLAIR sequence; Wahlund scale for WMH)	No significant association between regional WMH and MCR across six brain regions in either cohort (null)
Nagamalla et al. (2024) ¹³	733	733 (56 / 677)	Cross-sectional	Mean age 73.6 years; 45% female; four cohorts (three community, one memory clinic)	MCR-Neuroimaging Consortium (LonGenity, GAIT, CCMA, TASCOG)	USA, France, Australia	Magnetic resonance imaging (FreeSurfer cortical thickness, hippocampal subfield volumes)	Widespread cortical atrophy across prefrontal, parietal, temporal, insular, and cingulate regions was associated with MCR; hippocampal

Authors (year)	N	Imaging-analysis N (MCR n / non-MCR n)	Design	Participant characteristics	Cohort / Setting	Country	Imaging modality	Key neuroimaging findings
								subfield atrophy was associated with amnesic mild cognitive impairment but not with MCR
Nallapu et al. (2025) ²⁸	1,987	1,987 (117 / 1,661)	Cross-sectional	Mean age 71.7 years; 48% female; seven cohorts	MCR-Neuroimaging Consortium (CCMA, LonGenity, EAS, TASCOG, NCGG-SGS, KES, GAIT)	USA, Australia, Japan, India, France	Magnetic resonance imaging (FreeSurfer volumetric measures; HYDRA weakly supervised clustering)	Three neuroanatomical subgroups were identified among participants with slow gait: Group C (slowest gait, smallest cortical and hippocampal volumes, highest MCR prevalence at 9.0%) likely represents a pathological subtype; Group A showed preserved brain volumes despite slow gait, suggesting non-neurological contributors
Noh et al. (2026) ⁹	87	87 (27 / 60; 44 healthy controls + 16 MCI)	Cross-sectional	Mean age 74.5 years; 73% female; community-dwelling	Busan community health centers	South Korea	Electroencephalography (resting-state, 19 channels, theta power and default mode network connectivity)	Increased frontal theta power and widespread default mode network connectivity were observed in participants with MCR, with the largest effects between MCR and healthy controls (Cohen's d = 1.24); note: non-standard MCR definition requiring objective mild cognitive impairment
Park et al. (2025) ²⁹	81	81 (31 / 50; comparator = MCI without slow gait)	Cross-sectional	Mean age 75.0 years; 52% female; memory clinic patients with mild cognitive impairment	Jeju National University Hospital dementia clinic	South Korea	Magnetic resonance imaging (automated WMH segmentation; FreeSurfer 7.0)	WMH volume was independently associated with MCR in patients with mild cognitive impairment (odds ratio 1.11; 95% confidence interval 1.01 to 1.22); WMH volume was more than two-fold higher in the MCR group (13.9 mL) compared to the group without MCR (6.7 mL)
Udina et al. (2021) ¹⁰	538	325 (32 / 293)	Cross-sectional	Mean age 76.6 years; 55% female; community-dwelling	Central Control of Mobility in Aging study	USA	Functional near-infrared spectroscopy (prefrontal cortex oxygenation during dual-task walking)	Higher prefrontal cortex hemoglobin oxygenation during walk-while-talking was observed in

Authors (year)	N	Imaging-analysis N (MCR n / non-MCR n)	Design	Participant characteristics	Cohort / Setting	Country	Imaging modality	Key neuroimaging findings
								participants with MCR compared to those without, driven by left-sided prefrontal channels ($p = 0.03$)
Vazquez et al. (2026) ¹⁵	1,772	1,772 (129 / 1,643)	Cross-sectional	Mean age 71.1 years; 50% female; four cohorts	MCR-Neuroimaging Consortium (LonGenity, TASCOG, NCGG-SGS, KES)	USA, Australia, Japan, India	Magnetic resonance imaging (Age-Related White Matter Changes scale for WMH; lacunar infarcts)	Global WMH score (adjusted odds ratio 1.07), frontal WMH score (adjusted odds ratio 1.23), basal ganglia WMH score (adjusted odds ratio 1.31), and basal ganglia lacunes (adjusted odds ratio 1.57) were independently associated with MCR
Wang et al. (2016) ³⁰	139	139 (38 / 101)	Cross-sectional	Mean age 66.6 years; 33% female; clinic and community	Kerala-Einstein study	India	Magnetic resonance imaging (T1, T2, FLAIR, susceptibility-weighted imaging; lacunar infarcts, cerebral microbleeds, WMH)	Frontal lacunar infarcts were strongly associated with MCR (adjusted odds ratio 4.67; 95% confidence interval 1.69 to 12.94); global WMH burden and cerebral microbleeds were not associated
Xie et al. (2024) ¹⁷	126	126 (42 / 84)	Cross-sectional	Mean age 66.1 years; 38% female; hospital inpatients	Seventh Medical Center, PLA General Hospital	China	Magnetic resonance imaging (WMH, lacunar infarctions, cerebral microbleeds, total CSVD burden score)	Total CSVD burden score, but not any single imaging marker alone, was independently associated with MCR
Yaqub et al. (2022) ⁴	3,025	2,553 (cohort-level: 231 MCRS / 2,600 unaffected / 132 MCI / 62 both; per-prodrome n within the 2,553 MRI sub-sample not reported)	Cross-sectional	Mean age 70.4 years; 55% female; population-based	Rotterdam Study	Netherlands	Magnetic resonance imaging and diffusion tensor imaging	Lower grey matter volume, lower hippocampal volume, higher WMH burden, and lower fractional anisotropy in normal-appearing white matter were associated with MCR; findings were comparable to but distinguishable from mild cognitive impairment
Zhang et al. (2024) ³¹	2,540	661 (36 / 625)	Cross-sectional	Mean age 70.5 years; 57% female; population-based	Multimodal Interventions to Delay Dementia and Disability in Rural China (MIND-China) hearing sub-study	China	Magnetic resonance imaging (hippocampal volume)	Greater hippocampal volume was associated with reduced likelihood of MCR; high-frequency hearing loss was

Authors (year)	N	Imaging-analysis N (MCR n / non-MCR n)	Design	Participant characteristics	Cohort / Setting	Country	Imaging modality	Key neuroimaging findings
								associated with increased likelihood of MCR (adjusted odds ratio 1.91; 95% confidence interval 1.39 to 2.63)
Zhao et al. (2023) ¹⁸	134	134 (38 / 96)	Cross-sectional	Mean age 64.6 years; 35% female; hospital outpatients	Seventh Medical Center, PLA General Hospital	China	Magnetic resonance imaging (Fazekas scale for white matter lesions)	White matter lesion severity was higher in participants with MCR compared to those without (descriptive); white matter lesions were not entered as predictors in the multivariable model

Abbreviations: DTI, diffusion tensor imaging; fNIRS, functional near-infrared spectroscopy; EEG, electroencephalography; PET, positron emission tomography; MCI, mild cognitive impairment; AD, Alzheimer’s Disease; GAIT, Gait and Alzheimer Interactions Tracking; KES, Kerala-Einstein Study; CCMA, Central Control of Mobility in Aging; EAS, Einstein Aging Study; TASCOG, Tasmanian Study of Cognition and Gait; NCGG-SGS, National Center for Geriatrics and Gerontology Study of Geriatric Syndromes; MCR, motoric cognitive risk; PLA, People’s Liberation Army; MIND-China, Multimodal Interventions to Delay Dementia and Disability in Rural China; FLAIR, fluid-attenuated inversion recovery; WMH, white matter hyperintensities; CSVD, Cerebral Small Vessel Disease; HbO2, oxygenated hemoglobin; OR, odds ratio; aOR, adjusted odds ratio.

3.3. Risk of Bias

The Joanna Briggs Institute (JBI) Analytical Cross-Sectional Checklist ratings are presented in Figure 2. Eighteen studies (86%) were rated as low risk of bias, two (10%) as moderate risk, and one (5%) as high risk. The most common methodological concerns were the operationalization of MCR (Q3: unclear or no in 3 studies, reflecting non-standard gait thresholds in Zhao et al. (2023)¹⁸ and Xie et al. (2024)¹⁷ and the use of objective mild cognitive impairment rather than subjective cognitive complaints in Noh et al. (2026)⁹), incomplete adjustment for confounding factors (Q6: unclear or no in 3 studies), and lack of clarity regarding the validity of neuroimaging outcome measurement (Q7: unclear in 3 studies). The single high-risk study was Zhao et al. (2023)¹⁸, which used a non-standard gait assessment device and did not enter the neuroimaging variable into its multivariable model. The two moderate-risk studies were da Costa et al. (2025)²⁷, which had no control group and a non-significant primary outcome, and Xie et al. (2024)¹⁷, which used non-standard absolute gait-speed thresholds that inflated MCR prevalence to 33%. Raw agreement between the two reviewers was 90.5% (152/168 paired ratings across 21 papers × 8 JBI items). Inter-rater reliability was almost perfect (AC1 = 0.90).

3.4. Structural Correlates

3.4.1. Structural MRI: Volumetric and Cortical Thickness

Ten studies examined associations between MCR and brain volumes or cortical thickness. All ten reported lower volumes or thinner cortex in prefrontal regions among participants with MCR compared with those without^{3,4,7,11-14,19,28,31}. The most consistently affected regions were the prefrontal cortex, premotor and supplementary motor area, insula, and parietal cortices. Beauchet et al. (2016)⁷, in the GAIT study (N = 171), found that smaller volumes of total cortical gray matter, premotor cortex, and prefrontal cortex were associated with MCR, with the premotor cortex showing the largest between-group mean difference. Blumen et al. (2019)¹¹, using voxel-based morphometry and multivariate covariance analysis across three cohorts (N = 267), identified a grey matter volume network associated with MCR that included the supplementary motor area, insula, and prefrontal cortex. Blumen et al. (2021)¹², in a four-cohort consortium analysis (N = 199), reported pervasive cortical thinning in MCR across prefrontal, insular, temporal, and parietal regions, with cortical thickness showing greater sensitivity to MCR-related atrophy than cortical volume or surface area.

Hippocampal findings varied by study setting. Population-based community studies consistently reported smaller hippocampal volumes in MCR (Yaqub et al., 2022⁴, Rotterdam Study cohort N = 3,025; MRI sub-sample N = 2,553; Han et al., 2025¹⁴, MIND-China cohort N = 5,021; MRI sub-sample N = 1,159; Zhang et al., 2024³¹, MIND-China hearing sub-study cohort N = 2,540; MRI sub-sample N = 661), whereas studies based in memory clinics or pooled consortia without sex stratification did not^{7,13}. This discrepancy was resolved by Blumen et al. (2025)¹⁹ in a six-cohort sex-stratified analysis (N = 2,048), which demonstrated that MCR-related frontal atrophy was present in males but not females, whereas MCR-related hippocampal subfield atrophy

(involving CA1, subiculum, and the dentate gyrus) was present in females but not males. Nallapu et al. (2025)²⁸, in 1,778 slow-gait older adults pooled from seven cohorts, applied data-driven clustering to 41 brain-region volumes and identified three distinct neuroanatomical subgroups within the slow-gait pool (MCR prevalence 6.4 %, 7.4 %, and 9.0 %; $p < 0.001$). The highest MCR prevalence (9.0 %) was found in the subgroup with the slowest gait and the smallest cortical and hippocampal volumes, a classical neurodegenerative pattern, whereas a second subgroup had similarly slow gait but paradoxically larger volumes in some prefrontal and occipital regions and a lower MCR prevalence. The authors interpreted this as evidence that the MCR phenotype is neuroanatomically heterogeneous: an individual can reach the slow-gait criterion through a classical neurodegenerative pathway or through non-neurological factors such as musculoskeletal or cardiovascular deconditioning.

Studies directly comparing MCR and MCI within the same cohorts confirmed distinct structural signatures. Gomez et al. (2022)³ reported that MCR-associated atrophy was more pronounced in frontal and parietal regions, whereas MCI-associated atrophy was more pronounced in the temporal-parietal meta-region vulnerable to AD. Nagamalla et al. (2024)¹³ found that MCR was associated with a widespread cortical atrophy pattern affecting prefrontal, parietal, temporal, insular, and cingulate regions, whereas amnesic MCI was associated with restricted hippocampal subfield atrophy.

3.4.2. White Matter Hyperintensities and Cerebral Small Vessel Disease

Seven studies examined WMH or CSVD markers in relation to MCR^{8,15-18,29,30}. Six reported positive associations, while one reported null finding for all regional WMH measures. Studies employing quantitative volumetric WMH analysis or validated qualitative scales in large community-based samples consistently demonstrated positive associations. Doi et al. (2022)⁸, in the NCGG-SGS cohort ($N = 1,227$), reported that severe WMH (modified Fazekas grade 3–4) was associated with MCR after adjustment for demographic and vascular risk factors (OR 2.18, 95% CI 1.15–4.16). Vazquez et al. (2026)¹⁵, in a four-cohort consortium ($N = 1,772$), found that global WMH score, frontal WMH, and basal ganglia WMH were each independently associated with MCR (aOR 1.07–1.31), as were basal ganglia lacunes (aOR 1.57, 95% CI 1.08–2.27). Park et al. (2025)²⁹, in a sample of 81 patients with MCI, reported that automated WMH volume independently predicted MCR status (OR 1.11, 95% CI 1.01–1.22). Gomez et al. (2022)³ demonstrated in the ARIC study (cohort $N = 5,023$; MRI sub-sample $N = 1,591$) that the WMH burden associated with MCR was more than double that associated with MCI (143% greater).

By contrast, Mergeche et al. (2016)¹⁶, combining a French memory clinic cohort and an Indian community cohort ($N = 358$), found no association between regional WMH (rated on the Wahlund scale across six brain regions) and MCR in either cohort. Wang et al. (2016)³⁰, in the Kerala-Einstein study ($N = 139$), reported that frontal lacunar infarcts were strongly associated with MCR (aOR 4.67, 95% CI 1.69–12.94) but that global WMH burden and cerebral microbleeds were not. Xie et al. (2024)¹⁷, in a cohort of 126 CSVD inpatients, found that total CSVD burden (a composite score of lacunes, microbleeds, and Fazekas-graded WMH) independently predicted MCR, whereas individual markers alone did not.

3.4.3. Diffusion Tensor Imaging

Three studies examined white matter microstructure using DTI^{3,4,26}. All three reported greater microstructural damage in MCR compared to controls, with effects that were larger in magnitude than those observed in MCI. Gomez et al. (2022) found that MCR was associated with increased mean diffusivity in association, projection, and commissural white matter tracts, and decreased fractional anisotropy in commissural tracts³. Yaqub et al. (2022) reported lower fractional anisotropy and higher mean diffusivity in normal-appearing white matter in the Rotterdam Study⁴. Bommarito et al. (2022), in a pilot multimodal study ($N = 20$), found increased mean, axial, and radial diffusivity in the superior corona radiata of MCR participants, with preserved fractional anisotropy, a pattern more consistent with periventricular axonal compression than classical small vessel disease-related fiber disruption²⁶.

3.5. Functional Correlates

3.5.1. Functional Near-Infrared Spectroscopy and Electroencephalography

Three studies examined functional neuroimaging measures in MCR^{9,10,27}. Udina et al. (2021)¹⁰, using fNIRS during dual-task walking in the CCMA cohort (cohort $N = 538$; fNIRS sub-sample $N = 325$), reported higher prefrontal cortex oxygenation during the Walk While Talking condition in MCR compared to non-MCR participants (standardized HbO₂ 1.02 ± 1.25 vs. 0.66 ± 0.83 , $p = 0.03$), driven by left-sided prefrontal channels ($p = 0.017$). This pattern was interpreted as compensatory prefrontal hyperactivation, consistent with structural changes in prefrontal regions observed in the volumetric studies. da Costa et al. (2025)²⁷ examined prefrontal oxygenation during cycling exercise in 19 MCR participants without a control group and found a non-significant trend ($p = 0.124$), limiting inference about MCR-specific effects.

Noh et al. (2026)⁹, using resting-state EEG in a Korean community sample ($N = 87$), reported a graded increase in frontal theta power across healthy controls, MCI, and MCR groups, with the largest effect between MCR and controls (Cohen's $d = 1.24$). Theta-band default mode network connectivity was also greater in MCR than MCI. However, this study employed a non-standard MCR definition requiring objective cognitive impairment rather than subjective cognitive complaints, which limits direct comparability.

3.6. Molecular Correlates

3.6.1. Positron Emission Tomography

Two studies examined amyloid or tau PET in MCR^{3,26}. Neither found evidence of elevated AD pathology. Gomez et al. (2022)³ reported that amyloid deposition (florbetapir PET) was not elevated in MCR compared to controls (OR 1.63, 95% CI 0.47–6.53), in contrast to MCI, which showed nearly three-fold higher odds of amyloid positivity (OR 2.98, 95% CI 1.70–5.35). Bommarito et al. (2022)²⁶ found no differences in amyloid Centiloid values or tau PET standardized uptake value ratios between MCR and control participants.

3.7. Blood Biomarkers

Han et al. (2025)¹⁴ reported no associations between MCR and plasma amyloid- β 40, amyloid- β 42, total tau, or neurofilament light chain levels in the plasma biomarker subsample of the MIND-China study (N = 1,186), corroborating the PET findings and further supporting the absence of an AD molecular signature in MCR. These findings collectively distinguish MCR from MCI, in which biomarker evidence of AD pathology is consistently present.

4. Discussion

This systematic review synthesized neuroimaging evidence from 21 studies (total screening pool of 25,515 older adults; neuroimaging data available for 15,657) to characterize the brain structural, functional, and molecular correlates of MCR syndrome. Across multiple imaging modalities and diverse study populations, we identified a consistent pattern of frontoparietal-predominant cortical atrophy, involving prefrontal, premotor, insular, and parietal regions, that was reliably associated with MCR. WMH and CSVD markers were positively associated with MCR in community-based studies, and diffusion tensor imaging revealed widespread white matter microstructural disruption that exceeded that observed in mild cognitive impairment. Crucially, both PET and blood biomarker studies consistently found no evidence of elevated pathology in MCR, distinguishing the syndrome from MCI. Functional neuroimaging studies reported prefrontal hyperactivation during dual-task walking and altered EEG cortical activity, suggesting compensatory neural processes.

The most consistent finding across the reviewed studies was the association between MCR and reduced grey matter volume or cortical thickness in prefrontal, premotor, supplementary motor area, insular, and parietal regions. Ten structural MRI studies, encompassing community-based cohorts, population-based samples, and multicohort consortia, all reported smaller volumes or thinner cortex in these regions among individuals with MCR^{3,4,7,11-14,19,28,31}. The premotor cortex showed the largest effect size among the examined regions⁷, and multivariate covariance analysis identified a distributed grey matter network encompassing supplementary motor area, insula, and prefrontal cortex as the core structural signature of MCR¹¹. This consistent anatomical localization directly addresses the concern that MCR may represent only an operational definition without a clear biological substrate. When considered together with the white-matter, diffusion, and molecular evidence, these convergent structural findings advance a robust effort to delineate a unified neurobiological signature for the syndrome. That a brief clinical assessment, a subjective cognitive complaint combined with a timed walk, reliably identifies a replicable pattern of grey-matter network atrophy supports the view that MCR captures a distinct prodromal phenotype grounded in a frontoparietal neural pathway. These regions correspond closely to the “control pathway” of human locomotion, distinct from the motor execution pathway, and their involvement is consistent with the view that MCR reflects disruption of higher-order motor planning and cognitive control rather than primary motor dysfunction¹¹.

The association between MCR and CSVD markers further supports a vascular-predominant pathophysiology. Community-based studies using volumetric WMH quantification or validated qualitative scales consistently reported positive associations between greater WMH burden and MCR^{3,8,15,29}. The regional pattern of WMH involvement, predominantly frontal and basal ganglia, aligns with the frontoparietal atrophy pattern observed in volumetric studies. Lacunar infarcts, particularly in the frontal lobe and basal ganglia, were also independently associated with MCR^{15,30}, strengthening the case for cerebrovascular disease as a contributor to MCR pathophysiology. DTI findings corroborated this interpretation, with three studies reporting widespread white matter microstructural disruption in MCR, including increased mean diffusivity and decreased fractional anisotropy in association, projection, and commissural tracts^{3,4,26}.

The pattern of hippocampal involvement in MCR requires careful interpretation. Studies based in memory clinics or pooled consortia without sex stratification did not find significant hippocampal volume reduction in MCR^{7,13}, whereas population-based community studies consistently reported smaller hippocampal volumes^{4,14,31}. This apparent discrepancy is resolved by a recent large multicohort study that demonstrated sex-specific atrophy patterns in MCR: males showed frontal cortical thinning without hippocampal involvement, whereas females showed hippocampal subfield atrophy (involving CA1, subiculum, and the dentate gyrus) without frontal thinning¹⁹. This sex dissociation suggests that pooling sexes in previous analyses obscured two divergent neurobiological pathways to MCR, one frontal-predominant and more consistent with vascular pathology (males), and one hippocampal-predominant and more consistent with early AD-type pathology (females). This finding has implications for understanding sex differences in dementia subtype risk and for designing sex-stratified preventive strategies.

A notable finding of this review was the consistent absence of AD pathology in MCR. Two PET studies found no elevation of amyloid or tau burden in MCR^{3,26}, and a large population-based study reported no association between MCR and plasma amyloid- β , total tau, or neurofilament light chain levels¹⁴. These findings contrast sharply with MCI. In direct within-cohort comparisons, amyloid elevation was present only in MCI, not MCR³, and hippocampal atrophy was restricted to amnesic MCI, not MCR¹³. Taken together with the frontoparietal atrophy and WMH findings, these observations support the hypothesis that MCR represents a predominantly vascular-predominant or mixed-pathology prodrome, distinct from the classical AD pathway captured by MCI. However, the possibility that MCR may capture a subgroup of individuals who are amyloid-negative but progress to non-Alzheimer's dementias,

such as vascular dementia or dementia with Lewy bodies, warrants further investigation. It is also plausible that MCR and MCI represent partially overlapping rather than mutually exclusive populations, with some individuals meeting criteria for both syndromes^{3,4}.

Functional neuroimaging in MCR, though limited in scope, suggests the presence of compensatory neural processes. Using fNIRS during dual-task walking, Udina et al. (2021) found that MCR participants exhibited higher prefrontal cortex oxygenation during the Walk While Talking condition compared to non-MCR controls, driven by left-sided prefrontal channels¹⁰. This pattern is consistent with the scaffolding theory of aging⁶, which posits that increased prefrontal activation represents a compensatory response to declining neural structure and function. The finding is also consistent with structural changes in prefrontal regions observed across the volumetric studies and suggests that MCR participants may require greater neural effort to maintain dual-task performance. An EEG study reported increased frontal theta power and widespread default mode network connectivity in MCR, with effects most pronounced along the healthy control–MCI–MCR continuum⁹, though the non-standard MCR definition used in that study (requiring objective MCI rather than subjective cognitive complaints) limits direct comparability. Nevertheless, the striking functional cross-validation observed across these electrophysiological and haemodynamic modalities is notable. When challenged with dual-task demands, the brain in MCR consistently exhibits a distinct neurophysiological pattern of prefrontal hyperactivation and altered frontal theta power dynamics. This physiological strain suggests that structural network degradation directly impacts real-time cognitive–motor processing, providing a functional baseline that further solidifies the objective biological reality of the MCR syndrome.

The most common methodological concern was the heterogeneity of subjective cognitive complaint instruments across studies, which poses a significant threat to cross-study comparability. While some cohorts used the validated single-item Geriatric Depression Scale memory question, the same instrument used in the original MCR validation studies², others employed composite questionnaires, informant-based assessments, or self-report items whose psychometric properties in relation to MCR have not been established. Cohort overlap within the MCR Consortium was also identified as a concern, with several studies drawing from the same parent cohorts (GAIT, CCMA, NCGG-SGS), which limit the independence of the evidence base for certain findings. The use of harmonized image processing pipelines across consortium studies is a strength, but variability in scanner platforms, field strengths, and segmentation software across cohorts introduces unavoidable technical heterogeneity.

Limitations

This review has several limitations. First, all 21 included studies employed a cross-sectional design, no study reported a longitudinal neuroimaging analysis tracking change in brain structure or function over time, precluding inferences about the temporal sequence of neuroimaging changes and MCR onset. Longitudinal imaging studies are needed to determine whether the observed structural and vascular abnormalities precede, accompany, or follow the development of MCR. Second, no functional MRI studies of MCR were identified, representing a critical gap in the literature. Given that MCR involves both motor and cognitive domains, task-based and resting-state fMRI could provide valuable information about functional connectivity within the gait-control and default-mode networks. Third, only two small PET studies examined amyloid and tau pathology, and these were underpowered for subgroup analyses. Larger molecular imaging studies are needed to confirm the absence of AD pathology in MCR. Fourth, the evidence base is geographically skewed toward Asian (particularly Chinese and Japanese), European, and North American populations, with no studies from Africa or South America. Given that MCR prevalence and risk factor profiles may differ across populations, this limits the generalizability of the findings. Fifth, the substantial cohort overlap among MCR Consortium studies means that the effective independent sample size is smaller than the sum of individual study participants. Sixth, we did not conduct a quantitative meta-analysis due to the heterogeneity of outcome measures across modalities, which limits our ability to estimate pooled effect sizes.

Future Directions

Several priorities for future research emerge from this synthesis. Longitudinal imaging studies tracking structural, vascular, and molecular changes from the preclinical through the clinical stages of MCR to dementia are needed to establish temporal trajectories and identify biomarkers of progression. Standardization of subjective cognitive complaint instruments across cohorts would substantially enhance cross-study comparability. Future studies should routinely stratify analyses by sex, given the emerging evidence for sex-specific neural substrates. Larger amyloid and tau PET studies and expanded plasma biomarker panels are needed to confirm the absence of AD pathology and to explore other molecular pathways. Functional MRI studies, both task-based and resting-state, could clarify the functional brain networks underlying MCR. Also, EEG studies using standardized MCR criteria are needed, given that the current evidence base comprises a single small study; EEG's portability, low cost, and high temporal resolution make it particularly well-suited to scalable screening and to characterizing the compensatory cortical dynamics suggested by the existing fNIRS findings. Inclusion of underrepresented geographic regions, particularly Africa and South America, is essential to establish the generalizability of current findings.

Conclusions

This systematic review provides evidence that MCR is associated with a consistent neuroimaging signature characterized by frontoparietal-predominant cortical atrophy, WMH and microstructural damage, and the absence of AD pathology. This pattern is distinct from MCI and suggests a vascular-predominant or mixed-pathology prodromal pathway, with sex-specific neural substrates that may inform sex-stratified risk assessment. The findings highlight the potential of neuroimaging to differentiate predementia syndromes and to guide targeted preventive interventions.

Declarations

Conflict of Interest:

The authors declare no conflict of interest.

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References

1. Verghese J, Wang C, Lipton RB, Holtzer R (2013) Motoric cognitive risk syndrome and the risk of dementia. *Journals Gerontol Ser A: Biomedical Sci Med Sci* 68(4):412–418
2. Verghese J, Annweiler C, Ayers E et al (2014) Motoric cognitive risk syndrome: multicountry prevalence and dementia risk. *Neurology* 83(8):718–726
3. Gomez GT, Gottesman RF, Gabriel KP et al The association of motoric cognitive risk with incident dementia and neuroimaging characteristics: The Atherosclerosis Risk in Communities Study. *Alzheimer's Dement.* 2022;03/01 2022;18(3):434–444. <https://doi.org/10.1002/alz.12412>
4. Yaqub A, Darweesh SKL, Dommershuijsen LJ et al (2022) Risk factors, neuroimaging correlates and prognosis of the motoric cognitive risk syndrome: A population-based comparison with mild cognitive impairment. *Eur J Neurol* Jun 29(6):1587–1599. 10.1111/ene.15281
5. Studenski S, Perera S, Patel K et al (2011) Gait speed and survival in older adults. *JAMA* 2011/01/ 305(1):50–58. 10.1001/jama.2010.1923
6. Park DC, Reuter-Lorenz P (2009) The Adaptive Brain: Aging and Neurocognitive Scaffolding. *Annual Review of Psychology.* ;60(Volume 60, 2009):173–196. <https://doi.org/10.1146/annurev.psych.59.103006.093656>
7. Beauchet O, Allali G, Annweiler C, Verghese J (2016) Association of Motoric Cognitive Risk Syndrome With Brain Volumes: Results From the GAIT Study. *Journals Gerontology: Ser A* 71(8):1081–1088. 10.1093/gerona/glw012
8. Doi T, Nakakubo S, Tsutsumimoto K et al (2022) The association of white matter hyperintensities with motoric cognitive risk syndrome. *Cereb Circ Cogn Behav* 3:100150. 10.1016/j.cccb.2022.100150
9. Noh ES, Yang J, Wang K, Bae S, Park H (2026) Distinct patterns of cortical activity associated with cognitive and motor decline in community-dwelling older adults. *Exp Gerontol* Jan 213:113000. 10.1016/j.exger.2025.113000
10. Udina C, Ayers E, Inzitari M, Verghese J (2021) Walking While Talking and Prefrontal Oxygenation in Motoric Cognitive Risk Syndrome: Clinical and Pathophysiological Aspects. *J Alzheimers Dis* 84(4):1585–1596. 10.3233/jad-210239
11. Blumen HM, Allali G, Beauchet O, Lipton RB, Verghese J (2019) A Gray Matter Volume Covariance Network Associated with the Motoric Cognitive Risk Syndrome: A Multicohort MRI Study. *J Gerontol Biol Sci Med Sci* May 16(6):884–889. 10.1093/gerona/gly158
12. Blumen HM, Schwartz E, Allali G et al (2021) Cortical Thickness, Volume, and Surface Area in the Motoric Cognitive Risk Syndrome. *J Alzheimers Dis* 81(2):651–665. 10.3233/jad-201576
13. Nagamalla V, Verghese J, Ayers E et al (2024) Distinct Patterns of Brain Atrophy in Amnesic Mild Cognitive Impairment and Motoric Cognitive Risk Syndromes. *Neurodegenerative Dis* 24(3–4):117–128. 10.1159/000540512
14. Han X, Han Q, Wang X et al (2025) Clinical, biological, and neuroimaging profiles for motoric cognitive risk syndrome in older adults: The MIND-China study. *Journal of Internal Medicine.* /04/01 2025;297(4):409–422. <https://doi.org/10.1111/joim.20068>
15. Vazquez JP, Allali G, Beauchet O et al (2026) Cerebral small vessel disease unveils a vascular pathway to motoric cognitive risk in aging. *J Alzheimer's Disease* 109(3):1211–1219. 10.1177/13872877251405448
16. Mergeche JL, Verghese J, Allali G et al (2016) White Matter Hyperintensities in Older Adults and Motoric Cognitive Risk Syndrome. *J Neuroimaging Psychiatry Neurol* 1(2):73–78. 10.17756/jnpn.2016-009
17. Xie H, Zhang N, Xia C, Ding Y, Zhao H, Huang Y (2024) The clinical characteristics of cerebral small vessel disease patients with motoric cognitive risk syndrome during single- and dual-task walking. *Heliyon* 10(9):e30007. <https://doi.org/10.1016/j.heliyon.2024.e30007>. 2024/05/15/
18. Zhào H, Wei W, Xie H, Huang Y (2023) 2023;91(3):925–931 Motoric Cognitive Risk Syndrome Among Chinese Older Adults with White Matter Lesions: A Cross-Sectional Observational Study. *Journal of Alzheimer's disease: JAD.* 10.3233/jad-220712
19. Blumen HM, Delpratt N, Beauchet O et al (2025) Sex-specific brain atrophy patterns associated with the motoric cognitive risk syndrome. *J Alzheimers Dis* Nov 108(2):597–605. 10.1177/13872877251378656
20. Sekhon H, Allali G, Launay CP et al (2019) Motoric cognitive risk syndrome, incident cognitive impairment and morphological brain abnormalities: Systematic review and meta-analysis. *Maturitas* 123:45–54. <https://doi.org/10.1016/j.maturitas.2019.02.006>. 2019/05/01
21. Page MJ, McKenzie JE, Bossuyt PM et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372:n71. 10.1136/bmj.n71
22. Campbell M, McKenzie JE, Sowden A et al (2020) Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. *BMJ* 368:l6890. 10.1136/bmj.l6890

23. Moola S, Tufanaru C, Aromataris E et al (2019) Chapter 7: Systematic reviews of etiology and risk
24. Gwet KL (2008) Computing inter-rater reliability and its variance in the presence of high agreement. *Br J Math Stat Psychol* 05(1):29–48. <https://doi.org/10.1348/000711006X126600>. /01 2008
25. Landis JR, Koch GG (1977) The Measurement of Observer Agreement for Categorical Data. *Biometrics* 33(1):159–174. 10.2307/2529310
26. Bommarito G, Garibotto V, Frisoni GB et al (2022) The Biological Substrate of the Motoric Cognitive Risk Syndrome: A Pilot Study Using Amyloid-/Tau-PET and MR Imaging. *J Alzheimers Dis* 87(4):1483–1490. 10.3233/jad-215461
27. da Costa KG, Fontes EB, Menta A et al (2025) Prefrontal Cortex Oxygenation During Exercise in Older Adults with Motoric Cognitive Risk Syndrome. *Adv Biology* 9(6):2400231. <https://doi.org/10.1002/adbi.202400231>
28. Nallapu BT, Ezzati A, Blumen HM et al (2025) Discovering subtypes with imaging signatures in the Motoric Cognitive Risk Syndrome Consortium using weakly supervised clustering. *Alzheimers Dement (Amst)*. Oct-Dec 17(4):e70197. 10.1002/dad2.70197
29. Park JH, Yang HJ, Park S, Kim BS (2025) Greater White Matter Hyperintensities and More Severe Cognitive Dysfunction in Mild Cognitive Impairment With Motoric Cognitive Risk Syndrome. *J Korean Med Sci* Aug 25(33):e200. 10.3346/jkms.2025.40.e200
30. Wang N, Allali G, Kesavadas C et al (2016) Cerebral Small Vessel Disease and Motoric Cognitive Risk Syndrome: Results from the Kerala-Einstein Study. *J Alzheimers Dis* 50(3):699–707. 10.3233/jad-150523
31. Zhang Q, Zhao S, Feng J et al (2024) 2024;101(2):487–498 High-Frequency Hearing Loss, Hippocampal Volume, and Motoric Cognitive Risk Syndrome in Older Adults in China: A Population-Based Study. *Journal of Alzheimer's disease: JAD*. 10.3233/jad-240522

Figures

Identification of new studies via databases and registers

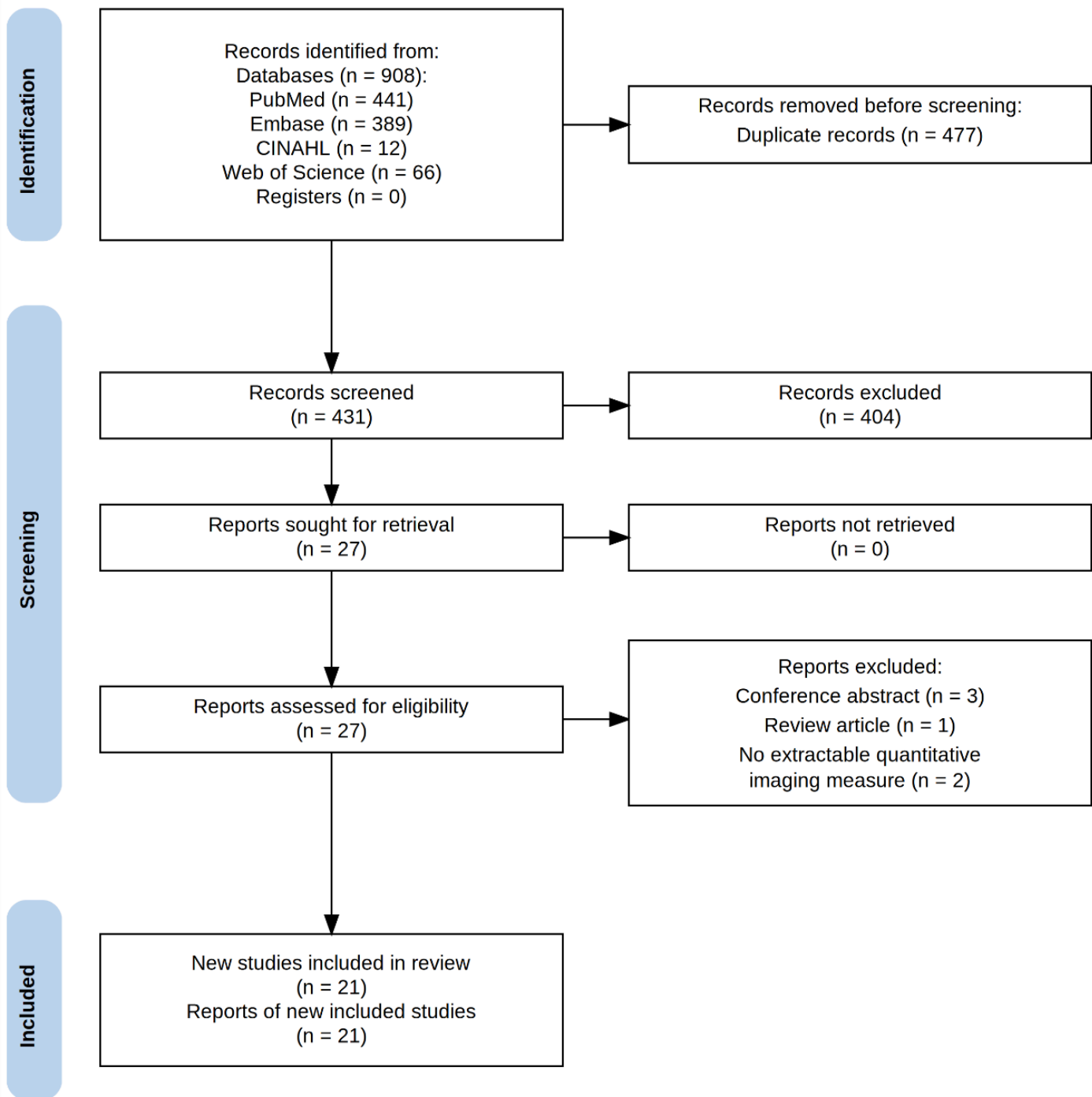


Figure 1

PRISMA 2020 flow diagram of study selection process.

A



B

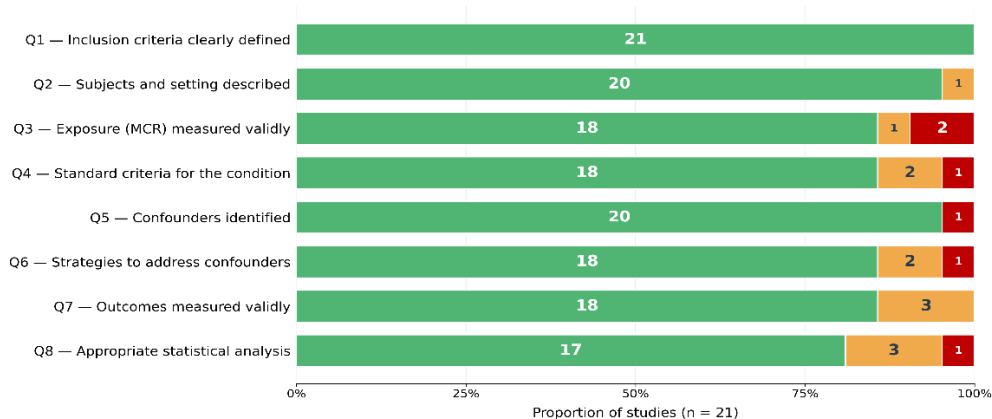


Figure 2

Risk of bias assessment using the Joanna Briggs Institute (JBI) Checklist for Analytical Cross-Sectional Studies. (A) Per-study traffic-light heatmap showing ratings for each of the eight JBI items (Q1–Q8), with the percentage of "Yes" ratings and the overall risk-of-bias judgement (Low, Moderate, High) shown for each study. (B) Item-level summary showing the proportion of studies rated Yes, Unclear, or No for each JBI item.

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